Mobile phone-based reminders for improving medication adherence in patients with common mental health disorders and determining the prescription pattern, cost and adverse effects – A randomized controlled trial

SYNOPSIS

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INTRODUCTION

According to the National Institute for Health and Care Excellence (NICE) guidelines, common mental health disorders include depression, generalised anxiety disorder, panic disorder, obsessive-compulsive disorder, social anxiety disorder and post-traumatic stress disorder. Approximately 15% of the population experiences common mental health disorders at any given time such as depression and anxiety. These conditions often involve cycles of relapse and recovery throughout a person's life.(1) A research on the global burden of disease (GBD) found that anxiety and depression rates in India were estimated at around 3.3% with a range of 3–3.5% for anxiety and 3.3% with a range of 3.1–3.6% for depression.(2) Antidepressants are the primary medication used to treat these common mental health disorders.(3),(4) Approximately fifty percent of individuals with psychiatric disorders in India do not adhere to their psychotropic medication.(5) The World Health Organization(WHO) has defined treatment adherence as "The extent to which a person's behaviour taking medication, following a diet, and/or executing lifestyle changes, corresponds with agreed recommendations from a healthcare provider".(6) Forgetting to take prescribed medicines was one of the most commonly reported causes for missing medication in following a treatment regimen. (7)To address issues of non-adherence, mobile phone technology is increasingly being utilised as part of 'mHealth' initiatives. These approaches aim to provide low-cost, sustainable healthcare solutions to patients with chronic illnesses (8).

Choosing the right antidepressant for a patient requires consideration of various factors like their demographics, the nature of their illness, possible medication side effects, any coexisting conditions, and the cost-effectiveness of the treatment.(9) Common mental disorders requiring ongoing treatment are linked to a mild degree of disability and impose a significant financial burden with substantial indirect costs. (10) It is crucial to investigate patient adherence to medication regimens for common mental health disorders, understand the reasons for non-adherence, analyse drug prescription patterns, evaluate economic impacts, and monitor adverse drug reactions. However, there is a significant lack of comprehensive studies in India. Conducting such research can offer valuable insights and aid in developing more effective strategies to enhance treatment adherence and clinical outcomes.

RESEARCH QUESTION

Do mobile phone -based Short Message Service (SMS) or voice call reminders in addition to usual treatment help to improve the medication adherence in common mental health disorders?

OBJECTIVES:

Primary objective:

1. To determine the effect of mobile phone voice calls or text messages in persistence and adherence to the treatment in patients with common mental health disorders.

Secondary objectives:

1. To determine the drug prescribing pattern in common mental health disorders.
2. To determine the reasons of non -adherence to the treatment in common mental health disorders.
3. To estimate the direct and indirect cost for the management of common mental health disorders for a period six months.
4. To determine the incidence of adverse drug reactions and to assess the causality, severity, predictability and preventability of adverse drug reactions of drugs used in the treatment of common mental health disorders.

REVIEW OF LITERATURE

People with mental health issues often struggle with treatment compliance, including remembering to take medication or attend appointments. Non-adherence to treatment can result in poor health outcomes, relapses, and hospitalisation. A cross-sectional study was conducted on 75 subjects by Sreejith et al. (2019) to elicit user needs, preferences and barriers to using mobile phones for healthcare service delivery among people with severe mental illness. Most patients reported using mobile phones and were favourably disposed to mHealth (mobile Health) approaches. Voice calls were the most preferred mode of service delivery. The most preferred service frequency was twice weekly, followed by once weekly. (11) A cross-sectional study done in five tertiary care psychiatric centres in India suggested that depressive disorders and anxiety disorders were the most common diagnoses where antidepressants were used. The most common antidepressant for depressive disorders was escitalopram, followed by sertraline. For anxiety disorders, escitalopram was most common, followed by paroxetine. For obsessive-compulsive disorder, fluoxetine and escitalopram were the predominant choices.(9) A comprehensive review concluded that patient-related factors such as forgetfulness, comorbidity, and misconceptions about the disease and medication; medication-related factors such as polypharmacy, side effects, pill burden, and cost; healthcare-system-related factors including the physician-patient interaction; sociocultural factors such as religious and cultural beliefs and stigma; and logistic factors were the major barriers to antidepressant adherence.(12) It is undeniable that antidepressants can cause Adverse Drug Reactions (ADRs). Although these medications generally have similar effects, there are differences in their safety profiles and the adverse reactions they may cause.

METHODOLOGY

Study design- Open-label rater blinded randomized controlled study

Sample size

The sample size was determined using GLIMMPSE version 2 from the University of Colorado, based on a group difference in slope of 0.5, a variance of random slopes of 1, the residual variance of 0.1, and a significance level of 0.05, aiming for a statistical power of 0.8. We planned to recruit 216 patients, distributed evenly across groups with 72 participants each, adjusting for a 10% attrition rate.

Inclusion criteria:

1. Patients diagnosed with any one common mental health disorder as per Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM -5), and in the age group of 18-65 years
2. Both male and female genders

Exclusion criteria:

1. Other psychiatric illnesses like bipolar depression, psychotic depression, organic mood disorders, substance-induced depression
2. Patients/caregivers who do not have access to mobile phones
3. Patients/caregivers who cannot read and understand either English or Tamil

Method of Recruitment and Allocation:

The study received approval from the institutional ethics committee (Ref No: IEC/2020/46) and was subsequently registered with the Clinical Trial Registry of India (CTRI) with reference number CTRI/2020/04/032949. Participant enrolment began in July 2020 and concluded in May 2023. All the patients who met the inclusion criteria and gave written informed consent during the study period were included. An open-label, rater-blinded, randomised, controlled trial was conducted to determine the effect of mobile phone-based interventions on adherence to medications in common mental health disorders. The patients were randomised into three groups using the

permuted block randomisation method. The sequence was generated by a person not involved in recruiting patients for the study. Allocation concealment was done using the serially numbered opaque sealed envelope technique. Patients were allocated into one control group and two intervention groups. Patients in the control group received treatment as usual for the entire study duration of six months. In the intervention groups, one group received SMS reminders, and the other group received voice calls (twice weekly for the first eight weeks and once weekly for the next eight weeks), followed by treatment alone for the remaining eight weeks. In the SMS reminder group, the SMS greeted the recipient, reminded them about taking medications at the prescribed times and doses, and ended with a positive message such as "Have a nice day." The message was sent between 9 am and 12 noon in English or Tamil, according to the patient's preference. The second intervention group received voice calls with pre-recorded messages between 9 am and 12 noon, where they were greeted and reminded about taking medications at the prescribed times and doses. The call ended with a positive message, "Have a nice day." Patients in the intervention groups also received a reminder for their follow-up visit five days before their next appointment. The standard treatment was given to all the patients at the clinician's discretion. No changes were made for the purpose of the study.

Data collection and Measurements and tools used

Basic and relevant sociodemographic data were collected from hospital records and reliable informants using a semi-structured proforma. The socioeconomic status was assessed using the Modified Kuppuswamy socioeconomic scale in 2019.(13) Medication persistence was assessed using the Refill Sequence Method. It was measured as the interval between the date of the first prescription and the point at which an unacceptable gap between prescription refills occurred. Thus, if a patient did not refill a prescription within a predetermined number of days (30 days), the patient was considered to have discontinued therapy and was thereafter classified as nonpersistent. (14)Medication adherence was evaluated using a multi-measure approach: the Medication Adherence Rating Scale (MARS) was used as a subjective measurement, and the Proportion of Days Covered (PDC) was used as an objective measurement. (15),(16)The Medication Adherence Reasons Scale (MAR-S) was used to determine the reasons contributing to non-adherence.(17)

To study the drug prescription pattern, details such as the names of prescribed medications, doses, strengths, frequencies, and durations of drug prescriptions were collected from the prescriptions entered into the Hospital Information Management System (HIMS). These details were collected at baseline and during every follow-up visit for six months. Cost analysis was conducted from the patient's perspective, including both direct and indirect costs, and was calculated over a period of six months. Patients were monitored for any adverse effects during each follow-up visit. Causality was assessed using the World Health Organization-Uppsala Monitoring Centre (WHO-UMC) causality Assessment Scale.(18) Severity was assessed using the Modified Hartwig and Siegel Scale. (19) Predictability was determined using the Rawlins and Thompson Scale.(20) Preventability was evaluated using the Schumock and Thornton Scale. (21)

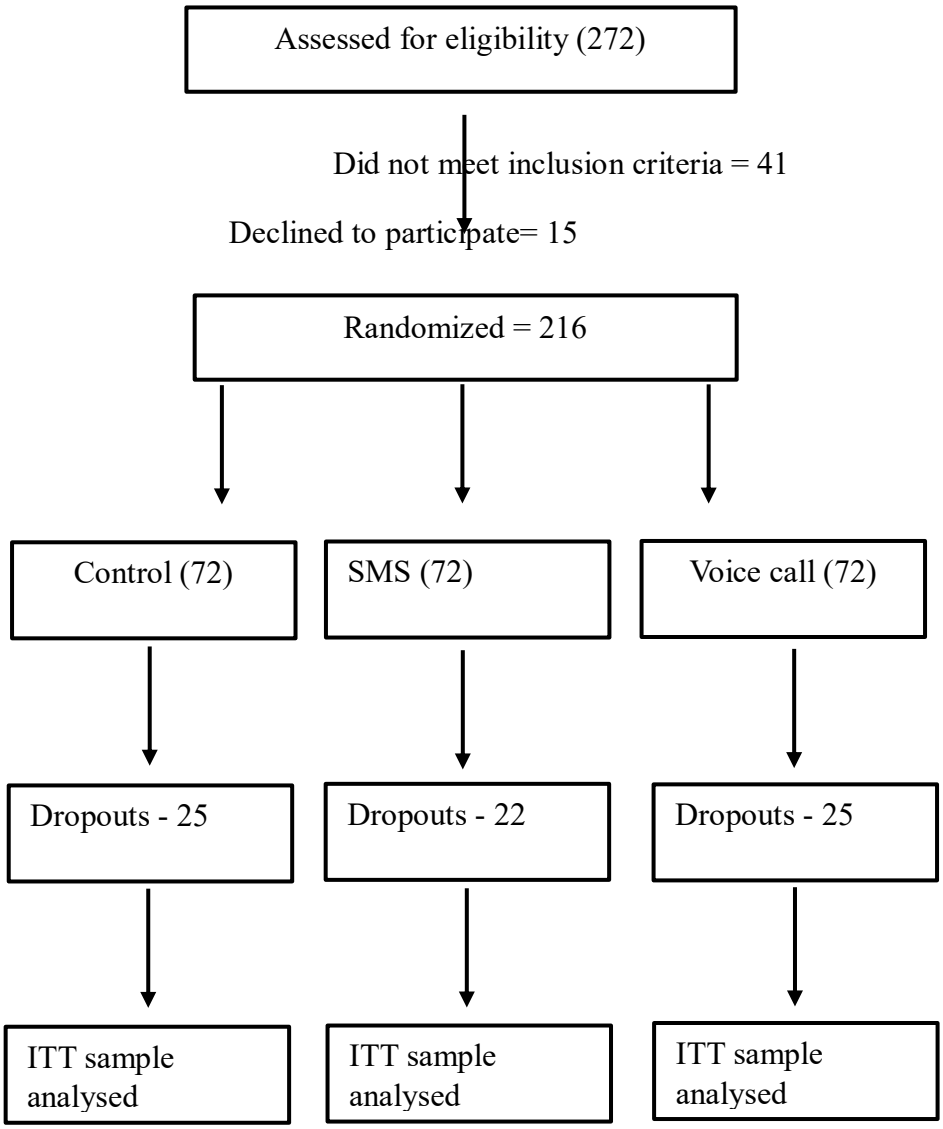
Statistical Analysis

All analyses were conducted on the Intention to Treat (ITT) sample using SPSS version 29. The Kolmogorov-Smirnov test was performed to assess the normality of the data. Descriptive statistics were used to summarise baseline demographics, clinical characteristics, and subgroups. The median and interquartile range (IQR) were used for continuous variables, while counts and proportions were used for categorical variables. Kruskal-Wallis test was performed to compare persistence and adherence (PDC and MARS scores). A P-value of less than 0.05 was considered statistically significant.

RESULTS

A total of 272 patients were assessed for eligibility to participate in the study and 216 were recruited. They were randomised into three groups (Control, SMS, Voice call) consisting of 72 participants in each group. Data was analysed utilising the intention-to-treat (ITT) method. The proportion of patients who dropped out of follow-up did not differ much among groups.

Figure 1: Consolidated Standards of Reporting Trials (CONSORT) flow diagram



Demographic characteristics of the patients were collected in a semi-structured proforma. Among 216 patients, 135 (62.5%) were females. Mean age was 38.76 ± 11.53. Most of the participants were married and resided in semi-urban areas. The socioeconomic status of the patients was assessed by the Modified Kuppusamy Socioeconomic Status Scale 2019. The majority of the patients were from the upper lower socioeconomic class (IV).

Table 1: Sociodemographic characteristics of patients with common mental health disorders

Characteristics	**Control (n=72, %)**	**SMS (n=72, %)**	**Voice call (n=72, %)**	**Overall (n=216, %)**
Age (years) Mean (SD)	39.74(12.38)	37.49(11.07)	39.06(11.14)	38.76(11.53)
Gender				
Male	25(34.72)	26(36.11)	30(41.67)	81(37.5)
Female	47(65.28)	46(63.89)	42(58.33)	135(62.5)
BMI Mean (SD)	24.57(4.48)	24.79(4.30)	24.89(5.03)	24.75(4.59)
Place of residence				
Urban	18(25.00)	10(13.89)	18(25.00)	46(21.29)
Semi-urban	25(34.72)	33(45.83)	32(44.44)	90(40.67)
Rural	29(40.28)	29(40.28)	22(30.56)	80(37.04)
Marital Status				
Unmarried	16(22.22)	14(19.44)	15(20.83)	45(20.83)
Married	46(63.89)	49(68.06)	52(72.22)	147(68.06)
Separated	3(4.17)	3(4.17)	1 (1.39)	7(3.24)
Divorced	4(5.56)	0(0.00)	0(0.00)	4(1.85)
Widowed	3(4.16)	6(8.33)	4(5.56)	13(6.02)
Socioeconomic Class				
Upper (I)	3(4.17)	6 (8.33)	3(4.17)	12(5.6)
Upper Middle (II)	22(30.56)	14 (19.44)	17 (23.61)	53(24.5)
Lower Middle (III)	21(29.16)	18 (25.00)	19 (26.39)	58(26.8)
Upper Lower (IV)	26(36.11)	33(45.84)	33(45.83)	92(42.6)
Lower (V)	0	1 (1.39)	0(0.00)	1(0.5)

Clinical characteristics of the patients were also collected in a semi-structured proforma. Among 216 patients, 146 were diagnosed with depressive disorders, and 70 were diagnosed with anxiety disorders. Data regarding their psychiatric illness, comorbidities, family history and details of substance abuse were collected.

Table 2: Clinical characteristics of patients with common mental health disorder

Characteristics	Control (n=72, %)	SMS (n=72, %)	Voice call (n=72, %)	Overall (n=216, %)
Diagnosis				
Depressive disorders	51(70.83)	48(66.67)	47(65.28)	146(67.59)
Anxiety disorders	21(29.17)	24(33.33)	25(34.72)	70(32.41)
Age of onset of illness (years) Median (IQR)	38(29,47)	34 (26,44)	37(26,45)	36(27,45)
Duration of illness (months) Median (IQR)	12(3,24)	12(4,36)	12(6,33)	12(4,36)
Duration of the current episode (months) Median (IQR)	4(1,8)	3(2,6)	5(2,12)	4(2, 7.8)
Substance Abuse				
Alcohol	1(1.39)	4(5.56)	3(4.17)	8(3.71)
Nicotine	1(1.39)	3(4.17)	2(2.78)	6(2.78)
Medical Comorbidities				
No comorbidities	46(63.89)	44(61.11)	43(59.72)	133(61.57)
Diabetes	5(6.94)	5(6.94)	12(16.67)	22(10.19)
Hypertension	10(13.89)	9(12.5)	14(19.44)	33(15.28)
Coronary Heart Disease	0(0.00)	0(0.00)	4(5.56)	4(1.85)
Dyslipidaemia	2(2.78)	0(0.00)	1(1.39)	3(1.39)
CKD	1(1.39)	0(0.00)	0(0.00)	1(0.46)
Chronic pain	1(1.39)	0(0.00)	2(2.78)	3(1.39)
Others	12 (16.67)	17(23.61)	8(11.11)	37(17.13)

Suicide attempts (if any)- Yes	11(15.28)	10 (13.89)	14(19.44)	35(16.2)
Inpatient admissions - Yes	1(1.389)	4(5.56)	8(11.11)	13(6.02)
Number of hospital days				
1-10	1(1.39)	1(1.39)	3(4.17)	5 (2.31)
11-20	0(0.00)	2(2.78)	2(2.78)	4 (1.85)
21-30	0(0.00)	0(0.00)	2(2.78)	2 (0.9)
31-40	0(0.00)	1(1.39)	1(1.39)	2 (0.9)
Family history of psychiatric illness- Yes	21(29.17)	12(16.67)	20(27.78)	53(24.54)
Family history of substance abuse				
Alcohol - Yes	3(4.17)	4(5.56)	3(4.17)	10(4.63)
Smoking- Yes	0(0.00)	1(1.39)	1(1.39)	2(0.93)

Medication persistence among the three groups was analysed using the refill sequence method. There was no significant difference in persistence between the groups.

Table 3: Comparison of Persistence among groups

Variables	Control (n=72) Median, IQR	SMS (n=72) Median, IQR	Voice call (n=72) Median, IQR	H value	P value
Persistence (in days)	43(15,100.5)	47.5(15,163.3)	41.5(15,139)	0.324	0.85

Medication adherence was evaluated through secondary database analysis as an objective measure, and the proportion of days covered was calculated. There was no significant difference among the three groups.

Table 4: Comparison of Proportion of Days Covered among groups

Variables	Control (n=72) Median, IQR	SMS (n=72) Median, IQR	Voice call (n=72) Median, IQR	H value	P value
Proportion of Days Covered	25(8,52.5)	25 (8,91.7)	19.5 (8,73.8)	0.177	0.915

MARS scores were compared among the three groups in the 4th week, 8th week, 16th week, and 24th week as a subjective measure. There was a statistically significant difference in the MARS score between the voice call group and the control group in 4th week. There was no difference in the MARS score among the three groups in the 8th week, 16th week and 24th week.

Table 5: Comparison of MARS scores among groups

Variables	Control		SMS		Voice call		P value
	N	Median IQR	N	Median IQR	N	Median IQR	
MARS score 4th week	46	6.5 (6,8)	46	7.0 (6.8,8.3)	44	8.0 (7,8)	0.02*
MARS score 8th week	29	8.0 (5.5,9)	32	8.0 (7.3,9)	31	8.0 (7,10)	0.17
MARS score 16th week	21	8.00 (6,10)	24	9.0 (7.3,10)	23	9.0 (8,10)	0.31
MARS score 24th week	20	8.00 (6,10)	20	9.0 (8,10)	19	9.0 (7,10)	0.17

* Compared between control and voice call

Data regarding the characteristics of the first prescription was collected. Among 216 prescriptions, 138 consisted of two medications. The mean duration of the first prescription is 13.7 +/- 6.5 days. Frequency of medication was found to be twice daily in 139 prescriptions.

Table 6: Characteristics of the first prescription issued in common mental health disorders

Variable	**Control n=72, (n%)**	**SMS n=72, (n%)**	**Voice call n=72, (n%)**	**Over all n=216, (n%)**
Number of medications				
1	30(41.67)	1(29.17)	22(30.56)	73(33.79)
2	41(56.94)	48(66.67)	49(68.06)	138(63.89)
3	1(1.39)	3 (4.16)	1(1.38)	5(2.31)
Duration of medication(days), mean (SD)	14.31(7.99)	13.99(5.97)	12.76(5.01)	13.69(6.45)
Frequency of medication				
Once daily	30(41.67)	22(30.55)	22(30.56)	74(34.26)
Twice daily	41(56.94)	48(66.67)	50 (69.44)	139(64.35)
Thrice daily	1(1.39)	2(2.78)	0 (0)	3(1.39)

Data regarding psychotropic medications at the first visit was collected. Sertraline was the most common medication, followed by escitalopram. Thus, SSRIs were the most commonly used class of medication. Benzodiazepines were the most commonly used additional drug.

Table 7: Primary psychotropic medications prescribed at the first visit among patients with common mental health disorders

Variable	Control n=72, (n%)	SMS n=72, (n%)	Voice call n=72, (n%)	Over all n=216, (n%)
Primary Medications				
Sertraline	27(37.5)	26 (36.11)	24 (33.33)	77 (35.65)
Escitalopram	23(31.95)	20 (27.78)	17 (23.61)	60 (27.78)
Mirtazapine	11(15.28)	9 (12.5)	12 (16.67)	32 (14.81)
Fluoxetine	6 (8.33)	10 (13.88)	10(13.89)	26 (12.04)
Venlafaxine	1(1.39)	2(2.78)	1 (1.39)	4 (1.85)
Dothiepin	3(4.16)	4 (5.56)	6 (8.33)	13(6.19)
Fluvoxamine	1(1.39)	0 (0)	1 (1.39)	2 (0.93)
Imipramine	0(0)	1 (1.39)	1(1.39)	2(0.93)
Additional Medications				
Benzodiazepines	37(51.39)	44(61.11)	47(65.28)	128(59.26)
Non benzodiazepines	5(6.94)	7(9.72)	3(4.17)	15(6.94)
No additional medication	30(41.67)	21(29.17)	22(30.56)	73(33.8)

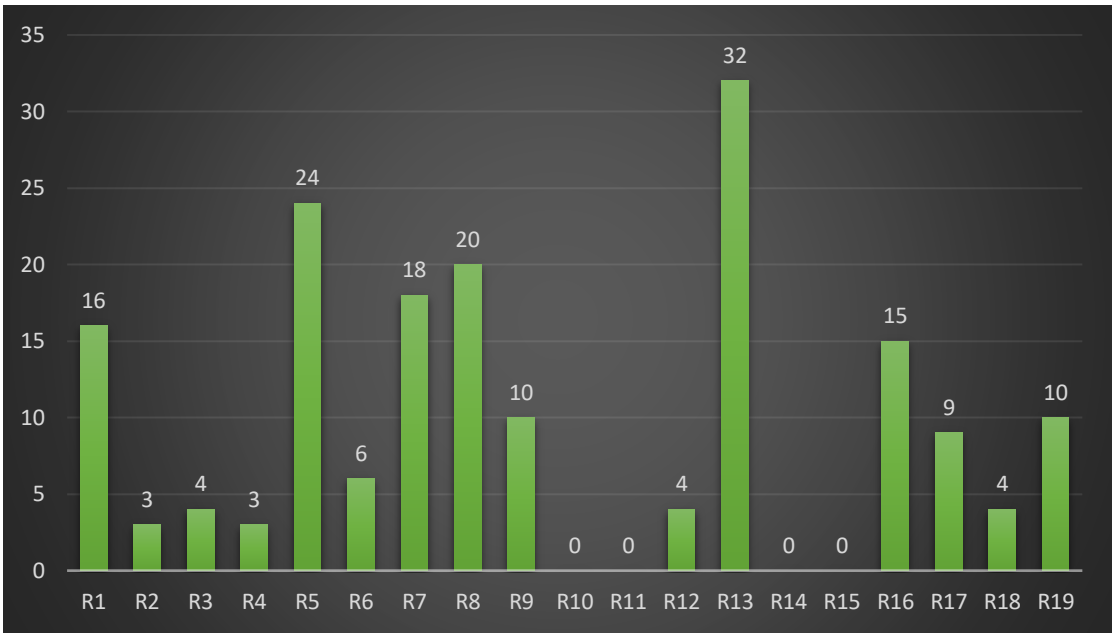
During the follow-up visits, primary medication was changed in 15 patients, an increase in dose was done in 105 cases, antidepressant combination therapy was found in 6 cases, and augmentation with non-antidepressant drugs was seen in 6 cases.

Table 8: Follow-up prescription in common mental health disorders during six month follow up period

Variable	Control n=72, (n%)	SMS n=72, (n%)	Voice call n=72, (n%)	Over all n=216, (n%)
Primary medication changed				
Yes	5(6.94)	6(8.33)	4(5.55)	15(6.94)
No	42(58.33)	44(61.11)	43(59.72)	129(59.73)
Not applicable	25(34.73)	22(30.56)	25(34.73)	72(33.33)
Increase in dose of primary medication				
Yes	36(50)	34(47.22)	35(48.61)	105(48.61)
No	11(15.27)	16(22.22)	12(16.66)	39(18.06)
Not applicable	25(34.72)	22(30.56)	25(34.72)	72(33.33)
Use of antidepressant combination therapy				
Yes	2(2.78)	2(2.78)	2(2.78)	6 (2.78)
No	45(62.5)	48(66.67)	45(62.5)	138(63.89)
Not applicable	25(34.72)	22(30.56)	25(34.72)	72(33.33)
Augmentation therapy with a non-antidepressant drug				
Yes	3(4.17)	2(2.78)	1(1.39)	6 (2.78)
No	44(61.11)	48(66.67)	46(63.89)	138(63.89)
Not applicable	25(34.72)	22(30.55)	25(34.72)	72(33.33)

The reasons for non-adherence are collected from the patients using the Medication Adherence Reasons Scale (MAR-S scale). The most common reasons for not adhering to medication were: the patient did not have a way to get to the pharmacy/provider, the patient thought they did not need the medication anymore, and concerns about possible side effects.

Figure 2: Reasons for nonadherence in patients with common mental health disorders



R1- I had side-effects from the medicine.

R2- I did not have money to pay for the medicine.

R3- I was not comfortable taking it for personal reasons (e.g. tired of taking medicine, too sick, my religious beliefs).

R4- I was not comfortable taking it for social reasons (e.g. I was with friends).

R5- I don't think that I need the medicine anymore.

R6- I don't think that the medicine is working for me.

R7 -I sometimes skip the medicine to see if it is still needed.

R8- I am concerned about possible side-effects from the medicine.

R9- I am concerned about long-term effects from the medicine.

R10- I had difficulty opening the container, or I had difficulty getting the injection ready to use (e.g., opening the package, mixing contents, drawing out the medicine)

R11- I had difficulty swallowing the medicine, applying the medicine, inhaling the medicine, or injecting the medicine (e.g., fear of needles, physical or sensory problems).

R12- I didn't have the medicine because the pharmacy/provider was out of this medicine, I was out of refills, or the mail order did not arrive in time

R13- I didn't have the medicine because I didn't have a way to get to the pharmacy/provider

R14- I am not sure how to take this medicine.

R 15-I have trouble managing all the medicines I have to take.

R 16 I would have taken it but have difficulty remembering things in my daily life.

R17- I would have taken it but missed it because of busy schedule/change in routine.

R18- I would have taken it but simply missed it.

R19- I do not consider taking the medicine as a high priority in my daily routine.

The cost incurred at baseline visit is expressed as median and IQR. Direct medical cost was ₹ 230.5(157.3, 418), direct non-medical cost was ₹ 250.0 (150,427.5), indirect cost was ₹ 200(100,437.5) and the total cost ₹ 899.5(594.8, 1634).

Table 9: **Cost analysis for baseline visits in patients with common mental health disorders**

Baseline cost	**Median (IQR)**
Direct medical cost	230.5(157.3, 418)
Direct non-medical cost	250.0 (150,427.5)
Indirect cost	200(100,437.5)
Total cost	899.5(594.8, 1634)

*All amounts are mentioned in Indian National Rupee

The six-month cost was analysed for those who completed months of treatment (42 patients). Direct medical cost ₹ 3346.5 (2572.5, 4530.8), direct non-medical cost was ₹ 1375(800, 2325), indirect cost was ₹ 1200(650, 2625) and the total cost ₹ 6723(4545.8, 10173.5).

Table 10: Cost Analysis for six months in patients with common mental health disorders

Six months cost	**Median (IQR)**
Direct medical cost	3346.5 (2572.5, 4530.8)
Direct non-medical cost	1375(800, 2325)
Indirect cost	1200(650, 2625)
Total cost	6723(4545.8, 10173.5)

*All amounts are mentioned in Indian National Rupee

Data on adverse drug reactions (ADRs) was collected from 144 patients who attended at least one follow-up visit. Among this group, 55 patients encountered at least one ADR, resulting in a total of 106 reported instances. The overall incidence rate of ADRs was determined to be 38.2%.

Table 11: Frequency of Adverse drug reactions during the treatment period

Name of the drug	**Number of patients receiving each drug**	**Number of patients with at least one ADR**	**Number of ADRs (n=106, %)**
Sertraline	56	21	37(34.9%)
Escitalopram	36	14	29(27.4 %)
Mirtazapine	25	9	18(16.9%)
Fluoxetine	15	6	15(14.2%)
Dothiepin	7	3	4(3.8%)
Venlafaxine	3	1	2(1.8%)
Imipramine	2	1	1(1%)
Total	144	55	106

The most commonly reported ADRs were weight gain (13 cases) followed by fatigue (11 cases), heartburn (10 cases) and indigestion (8 cases). The drug that most commonly led to weight gain was mirtazapine. Fatigue was widely reported with escitalopram.

Table 12: Adverse drug reaction profile in common mental health disorder treatment

Drug	Adverse drug reactions
Sertraline	Nausea (3), Heart burn (2), Indigestion (3), Constipation (2), Reduced appetite (3), Bloating (2), Dry mouth (1), Disturbed sleep (2), Headache (2), Fatigue (3), Dizziness (2), Drowsiness (1), Weight gain (3), Weight loss (1), Swelling of lips (1), Numbness over extremities (1), Loss of libido (1), Tremor (2), Breast pain (1), Pruritus (1).
Escitalopram	Nausea (2), Heartburn (4), Indigestion (4), Dry mouth (2), Disturbed sleep (1), Increased sleep onset (2), Headache (2), Fatigue (4), Dizziness (1), Drowsiness (3), Excessive sweating (1), Weight gain (3)
Mirtazapine	Heartburn (1), Indigestion (1), Dry mouth (1), Disturbed sleep (1), Fatigue (3), Drowsiness (2), Bitter taste (1), Weight gain (6), Increased urine frequency (1), Numbness over hand (1).
Fluoxetine	Nausea (1), Heart burn (2), Reduced appetite (1), Dry mouth (2), Fatigue (2), Drowsiness (1), Bitter taste (1), Disturbed sleep (1), Headache (1), Weight gain (1), Neck pain (1), Hair fall (1).
Dothiepin	Heartburn (1), Dry mouth (1) Increased heart rate (1), Premature ejaculation (1)
Venlafaxine	Reduced appetite (1), Constipation (1)
Imipramine	Tremor (1)

According to the WHO causality assessment criteria, 91 ADRs (85.8%) were classified as possible, while 15 ADRs (14.2%) fell into the probable category. In Hartwig's severity assessment scale, 67(63.2%) ADRs were classified as mild, while 39 (36.8%) were categorised as moderate. None of the ADRs was severe in nature. Out of the total 106ADRs, 97 (91.5%) adverse drug reactions were considered predictable, whereas 9 (8.5%) were unpredictable.

Table 13: Assessment of causality of Adverse drug reactions

Causality Assessment	Number of ADRs (n-106, %)
Probable	15(14%)
Possible	91(86%)

Table 14: Assessment of severity of Adverse drug reactions

Severity Assessment	Number of ADRs (n-106, %)
Mild	
Level 1	62(58.5%)
Level2	5(4.7%)
Moderate	
Level 3	39(36.8%)
Level 4	0(0%)
Severe	
Level 5,6,7	0(0%)

Table 15: Assessment of predictability of Adverse drug reactions

Predictability Assessment	Number of ADRs (n-106, %)
Predictable	97 (91.5%)
Not predictable	9(8.5%)

DISCUSSION

The present study evaluated the effect of mobile phone voice calls or text messages on persistence and adherence to the treatment in patients with 'common mental health disorders. In our study, there was no significant difference in persistence and adherence between the control and intervention groups. This may be because mobile phone reminders may improve persistence and adherence if forgetfulness is the reason for non-adherence. However, there can be other factors contributing to non-adherence in our patients. A pilot randomised controlled trial conducted in in South Africa found that the text message component did not significantly improve adherence in mental health service users with severe mental illness (22). Selective Serotonin Reuptake Inhibitors were the most commonly prescribed antidepressant class. A study investigated antidepressant prescription patterns for outpatients with depressive and anxiety disorders in a general hospital in Singapore, found that the most common antidepressant class was SSRIs, similar to our findings.(23) The primary reasons for medication non-adherence in our study were the patient didn't have a way to get to the provider, the belief that the medication was no longer needed, and concerns about potential side effects. An Evolutionary Concept Analysis on therapeutic adherence of people with mental disorders found that patients were less likely to follow the prescribed regimen if they did not believe in the effectiveness or necessity of the medication. Concerns about possible side effects, lack of insight into their condition, difficulty accessing healthcare services, and financial constraints prevented patients from adhering to their treatment plans.(24) In our study, direct cost was more than indirect cost. An Indian study analysed the cost of illness due to common mental health disorders and found that the indirect cost was more.(10) Our study revealed a 38.2% incidence rate of ADRs. The majority of reactions were possible in the WHO causality assessment. Many of these reactions were classified as mild on the severity assessment scale and predictable by Rawlings and Thompson's classification. A similar result was obtained in a cross-sectional study conducted in India. (25)

Limitations

1. Our study focused only on mobile phone-based reminders as an intervention for improving medication adherence. Other methods addressing various barriers to adherence were not explored.

2. The intervention was beneficial only if the patients or caregivers were literate and possessed a mobile phone.

3. The study was conducted in a single centre, so the generalizability of the findings to other settings may be limited.

4. The duration of follow-up in the study was six months, which may not address the long-term effects of interventions.

5. Blinding the participants was not feasible due to the nature of the intervention. However, rater blinding was done.

CONCLUSION

This randomised trial found no significant differences in persistence and adherence between the SMS, voice call and treatment as usual groups in patients with common mental health disorders. Non-adherence was mainly due to difficulties in reaching the medication provider, belief that medication was unnecessary, and concerns about side effects. SSRIs were the most commonly prescribed drug class. The study also noted higher direct costs for managing common mental health disorders. About one-third of patients experienced ADRs, with most of them classified as possible by the WHO causality assessment. According to the Hartwig severity assessment scale, most reactions were mild, and according to Rawlins and Thompson's classification, they were largely predictable.

These findings can help develop strategies to improve treatment adherence, patient safety, and clinical effectiveness. Managing common mental health disorders is challenging due to high rates of medication non-adherence, influenced by various reasons. The lack of significant difference in adherence between the control and intervention groups indicates mobile phone reminders alone are insufficient to improve medication adherence. The study suggests there are other important factors contributing to non-adherence in this patient population. A more comprehensive approach addressing the various barriers to adherence is necessary to enhance treatment outcomes in this population.

SUMMARY

According to NICE guidelines, approximately 15% of the population experiences common mental health disorders such as depression and anxiety at any given time. Proper medication adherence is crucial for effectively managing these disorders, with antidepressants being the primary treatment method. However, non-adherence remains a significant barrier to clinical effectiveness.

This research aimed to evaluate the effects of mobile phone reminders on medication adherence and treatment persistence in patients with common mental health disorders. Additionally, it sought to investigate factors leading to non-adherence, analyse drug prescribing patterns, estimate the direct and indirect costs of treatment over six months, and assess the incidence, causality, severity, predictability, and preventability of adverse drug reactions.

Patients were randomly assigned to one of three groups: a control group and two intervention groups. The control group received standard treatment throughout the study. One intervention group received SMS reminders, and the other received pre-recorded voice call reminders (twice weekly for the first eight weeks, then once weekly for the next eight weeks) alongside standard treatment, followed by treatment alone for the final eight weeks. Reminder messages for follow-up visits were sent to the intervention groups five days before their appointments.

Treatment adherence was evaluated as persistence and adherence. Persistence was measured using the refill sequence method, while adherence was assessed through the Medication Adherence Rating Scale (subjective) and secondary database analysis (objective). Reasons for non-adherence were identified using the Medication Adherence Reasons Scale. Drug prescribing patterns for common mental health disorders were observed over six months. Direct and indirect costs were collected using a semi-structured proforma. Adverse drug reactions were recorded during the follow-up period, and their causality, severity, predictability, and preventability were assessed.

A total of 272 patients were assessed for eligibility to include in the study, with 216 recruited and randomly assigned into three groups (Control, SMS, Voice call) of 72 participants each. Among these patients, 135 (62.5%) were female, with a mean age of 38.76 years (± 11.53). Most patients were from the upper lower socioeconomic class according to the Modified Kuppusamy Socioeconomic Status Scale 2019. Clinically, 146 patients were diagnosed with depressive disorders and 70 with anxiety disorders.

Medication persistence among the three groups was evaluated using the refill sequence method, with no significant differences found between the SMS, voice call, and treatment-as-usual groups for patients with common mental health disorders (P = 0.85). Medication adherence was assessed using both subjective (MARS score) and objective (proportion of days covered) measures. Secondary database analysis showed no significant differences in the proportion of days covered among the groups (P = 0.92). MARS scores were compared at the 4th, 8th, 16th, and 24th weeks. There was a statistically significant difference in MARS scores between the voice call group and the control group at the 4th week (P = 0.02). However, no significant differences were observed in MARS scores among the groups at the 8th (P = 0.17), 16th (P = 0.31), and 24th (P = 0.17) weeks.

Sertraline and escitalopram were the most commonly prescribed medications, with SSRIs being the predominant class of medication. Benzodiazepines were frequently used as additional drugs. Primary reasons for non-adherence included, the patient did not have a way to get to the pharmacy/provider, followed by the patient thought they did not need the medication anymore, and concerns about possible side effects. The most common reasons for not adhering to medication were: the patient did not have a way to get to the pharmacy/provider, the patient thought they did not need the medication anymore, and concerns about possible side effects. At the first visit, direct medical cost was ₹ 230.5 (IQR 157.3-418), direct non-medical cost was ₹ 250.0 (IQR 150-427.5), indirect cost was ₹ 200 (IQR 100-437.5), and total cost was ₹ 899.5 (IQR 594.8-1634). For the 42 patients who completed six months of treatment, costs were calculated as direct medical cost ₹ 3346.5 (IQR 2572.5-4530.8), direct non-medical cost ₹ 1375 (IQR 800-2325), indirect cost ₹ 1200 (IQR 650-2625), and total cost ₹ 6723 (IQR 4545.8-10173.5). Additionally, we found a 38.2% incidence rate of adverse drug reactions (ADRs). According to WHO criteria, 85.8% of ADRs were

classified as possible and 14.2% as probable. Severity assessment showed 63.2% mild and 36.8% moderate ADRs, with no severe cases. Additionally, 91.5% of ADRs were predictable.

In this randomised trial, there was no significant difference in persistence and adherence between the SMS, voice call and treatment as usual group. Primary reasons for non-adherence included difficulty in reaching the medication provider, followed by the belief that medication was unnecessary and concerns about side effects. Selective Serotonin Reuptake Inhibitors were the most commonly used drug class. This study revealed higher direct costs in the management of common mental health disorders. Additionally, we found a 38.2% incidence rate of adverse drug reactions (ADRs). The majority of reactions were possible in WHO causality assessment. Based on the Hartwig severity assessment scale, the majority of reactions were mild, and according to Rawlins and Thompson& classification, most were predictable.

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